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Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/732,163 | WARBURTON ET AL. | |
| | Examiner | Art Unit | |
| | Brian Whiteman | 1635 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *27 August 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1,3-7,9,10 and 13* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-7,9-10,13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

## DETAILED ACTION

### Final Rejection

Claims 1, 3-7,9-10, and 13 are pending.

Applicants' traversal, the amendment to claims 1, 3, and 13, the cancellation of claims 2 and 8 in paper no. 13 is acknowledged and considered.

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicants' submission filed on 1/3/03 has been entered.

### *Drawings*

Color photographs and color drawings are acceptable only for examination purposes unless a petition filed under 37 CFR 1.84(a)(2) is granted permitting their use as acceptable drawings. In the event that applicant wishes to use the drawings currently on file as acceptable drawings, a petition must be filed for acceptance of the color photographs or color drawings as acceptable drawings. Any such petition must be accompanied by the appropriate fee set forth in 37 CFR 1.17(h), three sets of color drawings or color photographs, as appropriate, and an amendment to the first paragraph of the brief description of the drawings section of the specification which states:

> The patent or application file contains at least one drawing executed in color. Copies of this patent or patent application publication with color drawing(s) will be provided by the U.S. Patent and Trademark Office upon request and payment of the necessary fee.

Color photographs will be accepted if the conditions for accepting color drawings have been satisfied.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3-7, 9-10, and 13 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1, 3-7, 9-10, and 13, as best understood, are readable on a genus of progenitor or stem cells capable of regenerating lung alveolar surface, wherein the genus of progenitor or stem cells are not claimed in a specific biochemical or molecular structure that could be envisioned by one skilled in the art at the time the invention was made are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification contemplates using a genus of progenitor or stem cells capable of regenerating lung alveolar surface. Furthermore, the specification contemplates that a species of stem/progenitor cells exist in the distal lung and can regenerate both alveolar epithelium and capillaries. The invention contemplates exploiting the properties of the stem cells by stimulating

them to divide and differentiate using soluble growth factors and other suitable growth factors (see page 9 of the specification). However, the specification only discloses *in vitro* embryonic day 12 (E12) lung cells cultured with FGF-10 and lung sections from embryonic and neonatal mice and hyperoxia treated adult rats express telomerase that plays a role in directional outgrowth and possibly induction of epithelial buds. The art of record displays a table of stem cells and the type of cell types developed and none of the stem cells developed into lung cells (NIH: News: Stem Cells; Stem Cells; Scientific Progress and Future Research Directions [online], June 2001, Appendix D, http://www.nih.gov/news/stemcell/scireport.htm, retrieved on 5/15/02). The specification does not disclose how to obtain or make a representative number of stem/progenitor cells that can regenerate lung alveolar surface. It is apparent that on the basis of applicant's disclosure, an adequate written description of the invention defined by the claims requires more than a mere statement that it is part of the invention and reference to potential methods and/or cells that are essential for the genus of stem or progenitor cells as claimed; what is required is the knowledge in the prior art and/or a description as to the availability of a representative number of species of progenitor or stem cells that must exhibit the disclosed biological functions as contemplated by the claims.

It is not sufficient to support the present claimed invention directed to a genus of progenitor or stem cells capable of regenerating lung alveolar surface. The claimed invention as a whole is not adequately described if the claims require essential or critical elements, which are not adequately described in the specification and which is not conventional in the art as of applicant's effective filing date. Claiming unspecified progenitor and/or stem that must possess the biological properties as contemplated by applicant's disclosure without defining what means

will do so is not in compliance with the written description requirement. Rather, it is an attempt to preempt the future before it has arrived. (See *Fiers v. Revel*, 25 USPQ2d 1601 (CA FC 1993) and *Regents of the Univ. Calif. v. Eli Lilly & Co.*, 43 USPQ2d 1398 (CA FC, 1997)). Possession may be shown by actual reduction to practice, clear depiction of the invention in a detailed drawing, or by describing the invention with sufficient relevant identifying characteristics such that a person skilled in the art would recognize that the inventor had possession of the claimed invention. Pfaff v. Wells Electronics, Inc., 48 USPQ2d 1641, 1646 (1998). The skilled artisan cannot envision the detailed structure of a genus of progenitor or stem cells that must exhibit the contemplated biological functions, and therefore, conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the structures and/or methods disclosed in the as-filed specification. Thus, in view of the reasons set forth above, one skilled in the art at the time the invention was made would not have recognized that applicant was in possession of the claimed invention as presently claimed.

Applicant's arguments filed 1/3/03 have been fully considered but they are not persuasive for the following reasons: the as-filed specification fails to provide sufficient description of progenitor or stem cells capable of regenerating lung alveolar surface. The as-filed specification describes using a growth factor to stimulate telomerase expression in mice cells. However, the skilled artisan cannot envision the detailed structure of a genus of progenitor or stem cells that must exhibit the contemplated biological functions, and therefore, conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the structures and/or methods disclosed in the as-filed specification. In addition, the applicants' traversal (page 4) states that, "one of skill in the art can lean upon the action of telomerase to

study stem cell lines". This assertion displays that the specification did not possess a genus of progenitor or stem cells that can be used to stimulate the growth of lung alveolar surface. Thus, in view of the reasons set forth above, one skilled in the art at the time the invention was made would not have recognized that applicant was in possession of the claimed invention as presently claimed.

Furthermore, with respect to the traversal displaying a new use of known materials, the traversal is not found persuasive because the art of record teaches that claimed genus of stem or progenitor cells are not known materials. For example, the art of record teaches that, "What is not known is whether there is a population of more primitive stem cells that could regenerate the alveolar and bronchial epithelium after injury ...The discovery of epithelial lung stem cells would be important, not only of understanding the process of lung development, but also for assessing the process of lung tumors and for applying potential of somatic gene therapy" (IDS, Mason et al. page 355, 1997). Further support of the lack of written description is provided by the art of record stating, "The lung epithelium is composed of a number of specialized cell types whose lineage relationship has not been fully characterized. Therefore, the mechanisms by which pulmonary epithelium proliferate and terminally differentiate must be further investigated" (IDS, Magdaleno et al., page 367, 1998). Furthermore, the art of record provides a table of stem cells and the type of cell types developed and none of the stem cells developed into lung cells (NIH: News: Stem Cells; Stem Cells; Scientific Progress and Future Research Directions [online], June 2001, Appendix D, http://www.nih.gov/news/stemcell/scireport.htm, retrieved on 5/15/02). Therefore, the assertion that the claimed invention is a new method for using a known material is not found persuasive because the applicants have not provided sufficient description of a

representative number of species of progenitor or stem cells to sufficiently describe the genus of progenitor or stem cells capable of regenerating lung alveolar surface so that one skilled in the art at the time the invention was made would not have recognized that applicants were in possession of the claimed invention as presently claimed.

Claims 1, 3-7, 9-10, and 13 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

> Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in In re Wands, 858 F.2d 731, 8USPQ2d 1400 (Fed. Cir. 1988). They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

Specifically, since the claimed invention is not supported by a sufficient written description (for possession of a genus of progenitor or stem cells capable of regenerating lung alveolar surface), particularly in view of the reasons set forth above, one skilled in the art would not have known how to use and make the claimed invention so that it would operate as intended, e.g. regenerating lung alveolar surface in a mammal.

The field of the invention embraces a method of stimulating the growth of lung alveolar surface in a lung of a mammal comprising: providing progenitor or stem cells capable of regenerating lung alveolar surface; and administering said cells to said lung (complete or a fraction of a lung) in an amount sufficient to stimulate the growth of the lung alveolar surface, wherein the lung is *ex vivo* and then transplanting said lung into the mammal.

The state of the art for tissue restoration displays that cell transplants have been used in several areas, (Stocum et al., Wound Rep Reg, Vol. 6, pp. 276-290, 1998). Stocum teaches that over the past 50 years, we have made progress in our ability to replace body parts with devices, solid organs, and tissue transplants, or both (page 277). Such replacement parts, however, still pose significant biological problems, and they are not useful for all situations (page 277). Furthermore, Stocum teaches that providing reliable sources of cells for cell transplant is crucial issue that requires establishing culture banks or proliferating stem, progenitor, or differentiated cells that can be drawn on as required, as well as cell culture media that support the proliferation and differentiation of these cells (page 284).

Furthermore with respect to lung transplantation, the state of the art for lung transplantation has gained widespread acceptance as a therapeutic option for a diverse array of lung diseases as taught by Arcasov et al. (Medical Progress, Vol. 340, pages 1081-1091. Nonetheless, complications are frequent and result constraints on long-term preservation of graft function and patient survival (page 1081). The common complications are primary graft failure, airway complications, infection, acute rejection, and chronic rejection (pages 1087-1088). Lung transplantation that reaches its current clinical plateau largely through refinements in the selection of patients, operative techniques, and postoperative care (page 1088). Two major hurdles must be overcome to increase the applicability of lung transplantation and improve long-term results: the supply of donor organs must be increased to meet the demand, and chronic rejection must be more effectively prevented (page 1088).

In addition, with respect to lung stem cells, the state of the art as exemplified by Magdaleno et al., (Adv Pediatr, Vol. 45, pp. 363-96, 1998), Magdaleno teaches that before stem

cells can used for therapeutic purposes understanding tissue genetics and immunology is essential (pages 363-364). Animal models or repair provide some clues about which cells are the stem cells in the lung (page 373). However, this approach is complex and oftentimes it is difficult to identify the specific molecular events that govern lung cell gene expression (page 373). In the course of studying the evidence for specific stem cells in the lung, one consensus perpetually emerges: the processes of lung development, gene regulation, and injury repair are multi-step processes involving a concerted effort between extracellular and intracellular input to elicit proliferation and/or differentiation of specific epithelial cell types of the airways (page 388).

The disclosure provides working examples: Example 1 (pages 10-16) displays that exogenous fibroblast growth factor 10 (fgf10) can stimulate wild type lung morphogenesis and rescues cells that were exposed to nitrogen in an *in vitro* cultures of murine lung cells. Example 2 (pages 16-22) encompasses hyperoxia treatment of adult rat and fetal rat alveolar epithelial type 2 cells (AEC2) isolated in cell cultures. The results from example 2 show that telomerase activity is observed in rat fetal AEC2 and can be re-induced in adult AEC 2 following hyperoxic injury. Furthermore, the disclosure contemplates a method of inducing lung regeneration by autologous stem cell replacement, wherein the stem cells are genetically modified (pages 9-10).

The as-filed specification provides sufficient guidance for one skilled in the art to use exogenous fgf10 to stimulate growth in an *in vitro* culture of murine lungs cells. However, this does not reasonably extrapolate to the claimed invention because the as-filed specification fails to provide sufficient guidance in several critical areas which encompass: 1) how to make and/or use any progenitor or stem cells in the method of the claimed invention, 2) how to determine

what progenitor or stem cells are capable of regenerating lung alveolar surface, 3) how to remove a lung or portion thereof, 4) how to administer said cells to said lung or portion thereof, 5) what amount is sufficient to stimulate the growth of lung alveolar surface, 6) how to avoid a graft vs. host response in a mammal undergoing a lung transplant, and 7) how to transplant a lung into a mammal. The as-filed specification fails to provide sufficient guidance for how stimulating murine lung cells *in vitro* can reasonably correlate to any method for treating a mammal that needs growth of the lung alveolar surface using progenitor or stem cells in a method of cell therapy. In view of the art of record, which teaches, "drawing analogies from the studies performed in rodents to human lung development raises certain caveats, however, because lung development in humans differs from that observed in rodents, See pages L1197-L1198 (Applicants' own work, Driscoll et al., Am J Physiol Lung Cell Mol Physiol, Vol. 279, pp. 1191-98, 2000)." Furthermore, Driscoll teaches that, "the data presented in the disclosure raises question to whether telomerase expression in the repairing lung is simply a marker for proliferation and whether it is expressed more ubiquitously than would be expected for a stem cell population (page L1196)." In addition, Driscoll teaches that, "because no method exist at the time the application was filed an currently for following the fate of individual cells in the lung, it is impossible to determine when and how telomerase expression is induced an how long it persists in each individual cell (page L1197)." In view of In Re Wands Factors, it would take one skilled in the art an undue amount of experimentation to reasonably correlate from the disclosure to any stem cell therapy method for stimulating the growth of the lung alveolar surface in a mammalian lung for a therapeutic result and transplanting lung back into a mammal. In view of the concerns stated by the art of record, the as-filed specification does not provide

sufficient guidance for one skilled in the art to make and/or use any progenitor or stem cells in any method of stimulating the growth of lung alveolar surface in any mammal's lung. Thus, in view of the In re Wands Factors, the disclosure is not enabled for the claimed invention.

In addition, with respect to claims 1, 3-7, and 9-12, the specification fails to provide what stem cells or progenitor cells are capable of regenerating lung alveolar surface in any mammal. The specification states that, "there are stem cells in the distal portion of the lung that can regenerate alveolar epithelium," however, the disclosure fails to provide sufficient guidance for what cells are capable of regenerating alveolar epithelium. The as-filed specification contemplates that any growth factor may be used to carry out the claimed invention and cites art of record (page 9), which list several growth factors. However, the specification and the art of record do not list what growth factors are required to make the stem cells or progenitor cells into cells that can be used in any method to stimulate the growth of lung alveolar surface. In view of the art of record (Stocum, pages 284-285), one skilled in the art understands that culturing stem cells into specialized cells (e.g. lung alveolar surface cells) would require an undue amount of experimentation in view of the art of record and the disclosure, since neither provides sufficient guidance for what growth factors and culture media is required to culture and support the proliferation and differentiation of any cells into cells that could be used in a method of stimulating the growth of lung alveolar surface.

Furthermore, with respect to using any progenitor or stem cells in any ex vivo method of cell therapy for stimulating the growth of lung alveolar surface, the as-filed specification fails to provide sufficient guidance for what type of progenitor or stem cells are capable of regenerating lung surface and how to circumvent the problem with the mammal's immune system when the

mammal is exposed to allogenic, xenogenic, or a genetically modified lung or portion thereof. See Stocum page 285, **Evasion of the immune system** and Arcaso, page 1086-1088, **common complications**.

In conclusion, the as-filed specification and claims coupled with the state of the art at the time the invention was made do not provide reasonable enablement for the claimed invention. In view of the state of the art for lung transplantation, stem cell therapy, wherein the stem cells are used in a cell therapy method, wherein the method is employed to correct a genetic disorder in any mammal was unpredictable at the time the invention was made, the lack of sufficient guidance to any therapeutic method of stem cell therapy, the breadth of the claims, one skilled in the art could not make and/or use the invention without undue experimentation.

Applicants' traversal filed on 1/3/03 is acknowledged and is not found persuasive for the following reasons: With respect to lung transplantation, the state of the art for lung transplantation has gained widespread acceptance as a therapeutic option for a diverse array of lung diseases as taught by Arcasov et al. (Medical Progress, Vol. 340, pages 1081-1091. Nonetheless, complications are frequent and result constraints on long-term preservation of graft function and patient survival (page 1081). The common complications are primary graft failure, airway complications, infection, acute rejection, and chronic rejection (pages 1087-1088). Lung transplantation had reached its current clinical plateau largely through refinements in the selection of patients, operative techniques, and postoperative care (page 1088). Two major hurdles must be overcome to increase the applicability of lung transplantation and improve long-

term results: the supply of donor organs must be increased to meet the demand, and chronic rejection must be more effectively prevented (page 1088).

In addition, with respect to lung stem cells, the state of the art as exemplified by Magdaleno et al., (Adv Pediatr, Vol. 45, pp. 363-96, 1998), Magdaleno teaches that before stem cells can used for therapeutic purposes understanding tissue genetics and immunology is essential (pages 363-364). Animal models or repair provide some clues about which cells are the stem cells in the lung (page 373). However, this approach is complex and oftentimes it is difficult to identify the specific molecular events that govern lung cell gene expression (page 373). In the course of studying the evidence for specific stem cells in the lung, one consensus perpetually emerges: the processes of lung development, gene regulation, and injury repair are multi-step processes involving a concerted effort between extracellular and intracellular input to elicit proliferation and/or differentiation of specific epithelial cell types of the airways (page 388).

Furthermore, the state of the art for tissue restoration displays that cell transplants have been used in several areas, (Stocum et al., Wound Rep Reg, Vol. 6, pp. 276-290, 1998). Stocum teaches that over the past 50 years, we have made progress in our ability to replace body parts with devices, solid organs, and tissue transplants, or both (page 277). Such replacement parts, however, still pose significant biological problems, and they are not useful for all situations (page 277). Furthermore, Stocum teaches that providing reliable sources of cells for cell transplant is crucial issue that requires establishing culture banks or proliferating stem, progenitor, or differentiated cells that can be drawn on as required, as well as cell culture media that support the proliferation and differentiation of these cells (page 284).

In addition with respect to the working examples in the as-filed specification teaching the growth of mouse lungs cells in the presence of a growth factor, the art of record teaches, "drawing analogies from the studies performed in rodents to human lung development raises certain caveats, however, because lung development in humans differs from that observed in rodents, See pages L1197-L1198 (Driscoll et al., Am J Physiol Lung Cell Mol Physiol, Vol. 279, pp. 1191-98, 2000)." Furthermore, Driscoll teaches that, "the data presented in the disclosure raises question to whether telomerase expression in the repairing lung is simply a marker for proliferation and whether it is expressed more ubiquitously than would be expected for a stem cell population (page L1196)." Therefore, in view of the In re Wands Factors, it would take one skilled in the an undue amount of experimentation to reasonably correlate the growth of mouse lungs cells using a particular growth factor to using a genus of stem or progenitor cells in a method of regenerating lung alveolar surface in a mammal.

Furthermore, the art of record teaches that claimed genus of stem cells was not known material. For example, the state of the art teaches that, "What is not known is whether there is a population of more primitive stem cells that could regenerate the alveolar and bronchial epithelium after injury ...The discovery of epithelial lung stem cells would be important, not only of understanding the process of lung development, but also for assessing the process of lung tumors and for applying potential of somatic gene therapy" (IDS, Mason et al. page 355, 1997). Further support of the lack of enablement for making and/or using genus of claimed stem cells is provided by the art stating, "The lung epithelium is composed of a number of specialized cell types whose lineage relationship has not been fully characterized. Therefore, the mechanisms by which pulmonary epithelium proliferate and terminally differentiate must be further

investigated" (IDS, Magdaleno et al., page 367, 1998). Furthermore, the state of the art provides a table of stem cells and the type of cell types developed and none of the stem cells developed into lung cells (NIH: News: Stem Cells; Stem Cells; Scientific Progress and Future and Research Directions [online], June 2001, Appendix D, http://www.nih.gov/news/stemcell/scireport.htm, retrieved on 5/15/02). In addition, Kotton et al.; Grove et al.; and Krause et al. are post-filing references and will not be considered. Therefore, the assertion that the claimed invention is a new method for using a known material is not found persuasive because the applicants have not provided sufficient description of a representative number of species of progenitor or stem cells to sufficiently provide guidance and/or factual evidence for the genus of progenitor or stem cells capable of regenerating lung alveolar surface.

It is the specification, not the knowledge of one skilled in the art that must supply the novel aspects of an invention in order to constitute adequate enablement, e.g. Genetech Inc. v. Novo Nordisk A/S, 108 F.3d 1361, 1366, 42, USPQ2d 1001, 1005 (Fed. Cir. 1997).

Furthermore, with respect to the assertion that the state of the art is such that USPTO can not properly shift the burden of establishing enablement to the applicant..

The court in Enzo 188 F.3d at 1374, 52 USPQ2d at 1138 states:

> It is well settled that patent applications are not required to disclose every species encompassed by their claims, even in an unpredictable art. However, there must be sufficient disclosure, either through illustrative examples or terminology, to teach those of ordinary skill how to make and use the invention as broadly as it is claimed.
> In re Vaeck, 947 F.2d 48, 496 & n.23. 30 USPQ2d 1438, 1445 &n23 (Fed. Cir. 1991)(citation omitted). Here, however, the teachings set forth in the specification provide no more than a "plan" or "invitation" for those of skill in the art to experiment...; they do not provide sufficient guidance or specificity as to how to execute that plan. See Fiers v. Revel. 984 F.2d.1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993); In re Wright, 999 F.2d...[1557], 1562, 27 USPQ2d...[1510], 1514. [Footnote omitted].

On this record, it is apparent that the specification and the applicants' traversal

(See pages 3-4 of the traversal, which states, "the patent specification need not teach and preferably omit what is well known in the art" and "one of skill in the art can lean upon the action of telomerase to study stem cell lines") provide no more than a plan or invitation in view of the art of record exemplifying the unpredictability of using any claimed method comprising stem cell therapy, for those skilled in the art to experiment with any progenitor or stem cell so as to provide regeneration of lung alveolar surface as intended by the as-filed specification at the time the invention was made.

See also Genetech Inc. v. Novo Nordisk A/S, 108 F.3d 1361, 1366, 42, USPQ2d 1001, 1005 (Fed. Cir. 1997)

> ("Tossing out the mere germ of an idea does not constitute enabling disclosure. While every aspect of a generic claim certainly need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable the public to understand and carry out the invention.")

In view of the art of record and the lack of guidance provided by the specification; the specification does not provide reasonable detail for what protocols are required for different types of stem cells for use in any method of stem cell therapy contemplated by the claimed invention, and it would take one skilled in the art an undue amount of experimentation to reasonably extrapolate from the assertion in the specification to the full breadth of the claimed invention. Therefore, the as-filed specification is not enabled for the claimed invention.

In addition, with respect to claims 1, 3-7, and 9-12, the specification fails to provide what stem cells or progenitor cells are capable of regenerating lung alveolar surface in a mammal. The specification states that, "there are stem cells in the distal portion of the lung that can regenerate alveolar epithelium," however, the disclosure fails to provide sufficient guidance for what cells are capable of regenerating alveolar epithelium. The as-filed specification

contemplates that any growth factor may be used to carry out the claimed invention and cites art of record (page 9), which list several growth factors. However, the art of record does not list what growth factors are required to make the stem cells or progenitor cells into cells that can be used in a method to stimulate the growth of lung alveolar surface in a mammal. In view of the art of record (Stocum, pages 284-285), one skilled in the art understands that culturing stem cells into specialized cells (e.g. lung alveolar surface cells) would require an undue amount of experimentation in view of the art of record and the disclosure, since neither provides sufficient guidance for what growth factors and culture media is required to culture and support the proliferation and differentiation of any cells into cells that could be used in a method of stimulating the growth of lung alveolar surface.

Therefore, in view of the In re Wands Factors, the claimed invention is not enabled because in view of the art of record and the undue amount of experimentation required to make and/or use the claimed invention; the lack of guidance or direction provided for making and/or using a representative number of stem or progenitor cells for regenerating lung alveolar surface in a mammal; the undue amount of experimentation to reasonably correlate the growth of mouse lungs cells using a particular growth factor to using a genus of stem or progenitor cells in a method of regenerating lung alveolar surface in a mammal; the unpredictability of lung transplant, stem cell therapy; different factors required for culturing different species of progenitor or stem cells; avoiding the mammal's immune response to said cells; the skill of those in the art was low; and the breadth of claims reading on using any type of progenitor or stem cells for regenerating lung alveolar surface.

***Conclusion***

All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Whiteman whose telephone number is (703) 305-0775. The examiner can normally be reached on Monday through Friday from 7:00 to 4:00 (Eastern Standard Time), with alternating Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's

supervisor, John L. LeGuyader, SPE - Art Unit 1635, can be reached at (703) 308-0447.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number is (703) 308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Brian Whiteman
Patent Examiner, Group 1635

Scott D. Priebe

SCOTT D. PRIEBE, PH.D
PRIMARY EXAMINER